

## ABSTRACT

The present invention relates generally to the fields of genetics, biochemistry, medicinal chemistry and medicine. The present invention more particularly discloses the identification of a human gene variant involved in neuropathological conditions, and methods for the diagnosis, prevention and treatment of such diseases and related disorders, as well as for the screening of therapeutically active drugs. The present invention relates to catalytically active beta-secretase (Memapsin2, BACE) variants, and nucleic acids encoding them. The invention is useful in the identification of agents that inhibit the activity of a particular BACE isoform and thus agents and therapies affecting the genesis, development or progression of neuropathological conditions, including Alzheimer's disease and dementia.